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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
09/016,061	01/30/98	HUSE	P-IX2965

EXAMINER: W

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HM22/0718

ART UNIT	PAPER NUMBER
1644	16

DATE MAILED: 07/18/00

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 5/1/00

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 56-104 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☑ Claim(s) _____ is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892

☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). 5/7/15

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

– SEE OFFICE ACTION ON THE FOLLOWING PAGES –

DETAILED ACTION

1. Applicant's election of Group I in Paper No. 14 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant's election without traverse of Group I (claims 56-97) and the antibody species 6H6 with the sequences referenced as SEQ ID NOS: 90/94 in Paper No. 14 is acknowledged.

Applicant submits that the elected species read on claims 56-59, 62, 65-68, 70-77, 84, 85, 90, 91 and 94-97.

Claims 1-55 have been canceled have been canceled previously.
Claims 56-104 are pending

Claims 60, 61, 63, 64, 69, 78-83, 92, 93 have been withdrawn from consideration by the examiner 37 CAR 1.142(b), as being drawn to a nonelected invention and/or species

Claims 56-59, 62, 65-68, 70-77, 84, 85, 90, 91 and 94-97 are under consideration in the instant application.

2. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed

3. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate corrections are required

4. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 56-59, 62, 65-68, 70-77, 84, 85, 90, 91 and 94-97:

It is apparent that the LM609 antibody is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the hybridoma which produces this antibody. See 37 CAR 1.801-1.809.

In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the original deposit is made after the effective filing date of an application for patent, the applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in which the case the statement need not be verified. See MPEP 1.804(b).

It is noted that if the claimed and disclosed amino acid sequences or nucleic acid sequences set forth in the instant application encode the entire LM609 antibody, then a deposit for said LM609 antibody (hybridoma) is not required. The sequence of an entire immunoglobulin satisfies the biological deposit of said immunoglobulin.

6. Claims 56-59, 62, 65-68, 70-77, 84, 85, 90, 91 and 94-97 are rejected under 35 U.S.C. § 112, first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention

The instant claims are indefinite in the recitation of ""enhanced LM609 grafted antibody" and "functional fragment thereof" because their characteristics are not known. This language is vague and indefinite since it encompasses many different amino acid (and nucleic acid sequences) as well as many different forms and modifications and it is not clear from the disclosure which particular "enhanced" or "function" are being referred to. There is insufficient information and guidance concerning the metes and bound of said "enhanced" and "function" as it relates to the structure and/or function of the LM609-specific antibodies (and nucleic acids) encoding said antibodies. The metes and bounds of said "enhanced" and "functional fragment thereof" have not been clearly defined in the specification as filed.

These terms are relative term which renders the claim indefinite. For example, pages 16-17, overlapping paragraph of the instant specification discloses that the functional characteristic of the antibody has been altered or augmented compared to a reference antibody, which can include both higher or lower affinity. Therefore, the claimed "enhanced LM609 antibody" can have contrasting properties and still be considered enhanced with respect to the referenced LM609 antibody. Further, the terms are not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of recombinant antibodies (and nucleic acids) encoding said recombinant antibodies broadly encompassed by the claims and the claims broadly encompass a significant number of inoperative species. Both CDRs and framework regions contribute to successful humanization of functional antibodies. An effective number of exposed amino acid residues in framework regions that are consistent with corresponding framework regions of a human antibody do not necessarily correlate with either reduced immunogenicity or functional retention. Often excising out portions of a protein or modifications to a protein would result in deleterious effects to the overall activity and effectiveness of a protein. Applicant has not clearly shown or define the criticality or permissibility of the modifications encompassed by the claims that result in "enhanced LM609 antibodies" and "functional fragment thereof" that provide enhanced LM609-specific antibodies and nucleic acids encoding said antibodies. Similarly, the absence of reciting a function would encompass undue experimentation in designing "enhanced LM609 antibodies" and "functional fragments thereof", wherein a number of different functions, not all of which are directed to the LM609 specificity and enhanced function intended by the instant invention.

It would require undue experimentation to produce all such possible recombinant antibodies (and nucleic acids) without more explicit guidance from the disclosure. It would require undue experimentation to investigate all such recombinant antibodies (and nucleic acids).

The applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter.

Applicant is invited to considered to amend the instant claims to distinctly claim specific functional or structural attributes of the claimed LM609 antibodies

7. Claims 56-59, 62, 65-68, 70-77, 84, 85, 90, 91 and 94-97 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 56-59, 62, 65-68, 70-77, 84, 85, 90, 91 and 94-97 are indefinite in the recitation of "LM609" because its characteristics are not known. The use of "LM609" monoclonal antibody as the sole means of identifying the claimed antibody renders the claim indefinite because "LM609" is merely a laboratory designation which does not clearly define the claimed product, since different laboratories may use the same laboratory designation to define completely distinct cell lines or hybridomas.

As pointed out above in Section 5, the disclosure of the sequence for an entire immunoglobulin satisfies the biological deposit of said immunoglobulin and would render the claims definite.

The amendments must be supported by the specification so as not to add any new matter. See MPEP 714.02 and 2163.06

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 56-59, 62, 65-68, 70-75, 77, 84, 85, 90, 91 and 94-97 are rejected under 35 U.S.C. § 102(e) as being anticipated by Brooks et al. (U.S. Patent No. 5,753,230; 1449). Brooks et al. teach the LM609 antibody as well as humanized forms of this antibody and claim methods of using the LM609 antibody as well as humanized forms of this antibody (see entire document, particularly columns 15-19 and the claims). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced LM609 antibodies and humanized antibodies thereof.

As pointed out above in Section 6; pages 16-17, overlapping paragraph of the instant specification discloses that the functional characteristic of the antibody has been altered or augmented compared to a reference antibody, which can include both higher or lower affinity. Therefore, the claimed "enhanced LM609 antibody" can have contrasting properties and still be considered enhanced with respect to the referenced LM609 antibody. Given the prior art teaching of humanized LM609 antibodies and that the claimed recitation of "enhanced LM609 antibody" encompasses a variety of modified forms of the LM609, provided it differs from the native LM609 antibody; the prior art humanized antibodies read on the claimed antibodies.

11. Claims 56-59, 62, 66-68, 70, 71, 74-76, are rejected under 35 U.S.C. § 103(a) as being unpatentable over Brooks et al. (U.S. Patent No. 5,753,230; 1449) in view of art known gene cloning and expression strategies for deriving recombinant antibodies and fragments thereof, as disclosed on pages 10-39 or Examples I and II of the instant specification or as cited by references on the 1449, including Queen et al. (5,585,089), Rosok et al. (J. Biol. Chem. 271: 22611-2618, 1996), Glaser et al. J. Immunol. 149: 3903-3913, 1992).

Brooks et al. teach the LM609 antibody as well as humanized forms of this antibody and claim methods of using the LM609 antibody as well as humanized forms of this antibody (see entire document, particularly columns 15-19 and the claims). With respect to specific amino acid changes including those which are encompassed by "enhanced LM609" would be obvious given the teachings of humanized LM609 antibodies and art known methods to generate such humanized antibodies which retain the desired functional characteristics of the native antibody and to alter said antibody for therapeutic uses, including human therapy, as taught and known in the prior art.

Therefore the primary references clearly teach $\alpha v\beta 3$-specific antibodies the instant LM609 specificity and associated properties as valuable diagnostic and therapeutic tools in various biological processes. These references differ from the instant claims by not disclosing the generation of recombinant forms and nucleic acids of the LM609 antibody and hybridoma per se.

Given the availability of the LM609 antibody and hybridoma together with general immunoglobulin gene cloning and expression strategies, it would have been have been a matter of routine experimentation well within the ordinary skill level of art to generate chimeric or humanized LM609 antibodies, DNA encoding said antibodies. Given the highly conserved nature of immunoglobulin gene organization and structure and the availability of probes and PCR primers for immunoglobulin gene cloning, one of ordinary skill in the art could have isolated the functionally rearranged heavy and light chain variable regions from the LM609 hybridoma cell line and determined their sequences with a complete expectation of success. For example, the ordinary artisan does not need to determine the amino acid sequences of a rearranged V (variable) region before cloning.

The claims do not differ unexpectedly or unobviously from what one of ordinary skill in the art would have expected to obtain given the known LM609 hybridoma thereof, the known heavy and light chain and the art known techniques regarding the production of chimeric antibodies, as acknowledged by the number of available art known procedures disclosed in the instant specification and cited on the Information Disclosure Statement. For example. Queen et al. teaches the art known method of producing humanized antibodies of interest at the time the invention was made. Also, Rosok et al. and Glaser et al. teach providing for the selecting recombinant antibodies of interest, including selecting for alterations of antibody affinity.

Immunoglobulin gene structure and organization were well understood in the art a the time the claimed invention was made and that strategies for cloning the DNAs encoding immunoglobulin variable regions genes were well established in the art at the time the claimed invention was made, as were methods for the production of DNA constructs encoding immunoglobulin variable regions. In addition, it was known at the time the invention was made that the benefits of producing recombinant antibodies to reduce the immunogenicity of therapeutic and diagnostic antibodies in human patients. Also, the ordinary artisan would have selected for modified recombinant forms of the art known LM609, including those with modifications that would have provided for either lower immunogenicity or altered affinity to enhanced the diagnostic/therapeutic potential of the LM609 antibody specificity with an expectation of success at the time the invention was made. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Given the breadth of the claims to read on the LM609 antibody, the instant antibodies and nucleic acids read on a genus of antibodies (and nucleic acids) encompassed by LM609 and modifications thereof.

12. Claims 56-59, 62, 65-68, 70-77, 84, 85, 90, 91 and 94-97 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18 and 26-31 of copending application USSN 08/790,540 and claims 1-8, 15-26, 33-42 of copending USSN 08/791,391.

Although the conflicting claims are not identical, they are not patentably distinct from each other because each application is drawn to the same or nearly the same LM609-specific antibodies (and nucleic acid) encoding said antibodies and modifications thereof.

The specific species recited in claims 65, 72, 73, 77, 84, 85, 90, 91, 94-97 which encompass specific amino SEQ ID NOS: 90 and 94 read as species on the genus of LM609-specific recombinant antibodies.

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Given that USSN 08/791,391 appears to have the same inventive entity as the instant application, USSN 08/790,540 does not appear to have the same inventive entity; the following is noted.

Claims 56-59, 62, 65-68, 70-77, 84, 85, 90, 91 and 94-97 are directed to an invention not patentably distinct from claims 1-18 and 26-31 of copending application USSN 08/790,540.

Commonly assigned USSN 08/790,540, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. § 103 if the commonly assigned case qualifies as prior art under 35 U.S.C. § 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 37 C.F.R. § 1.78© to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application. A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. § 103 based upon the commonly assigned case as a reference under 35 U.S.C. § 102(f) or (g).

13. No claim is allowed.

Claims 65, 72, 73, 77, 84, 85, 90, 91', 94-97 which recite specific amino SEQ ID NOS: 90 and 94 are considered free of the prior art, as the prior art does not appear to suggest these particular CDRs for LM609-specific recombinant antibodies.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, PhD.
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Technology Center 1600
July 17, 2000